DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-6 and 8-11 in the reply filed on 4/10/08 is acknowledged. The traversal is on the ground(s) that there appears to be no serious burden to search and examine all claims. This is not found persuasive because Applicant is referring to the requirement to demonstrate search burden that pertains to applications filed under 35 U.S.C. 111(a) (see MPEP 801). There is no corresponding requirement to demonstrate search burden in applications filed under 35 U.S.C. 371. Applicant also invokes MPEP 803; however, this section pertains to applications filed under 35 U.S.C. 111.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 7 and 12-15 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/10/08 as discussed above.

Priority

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

This application claims benefit to provisional application No. 60/542,201, filed on 2/5/04, in a language other than English. An English translation of the non-English language provisional

application and a statement that the translation is accurate must be filed in provisional application No. 60/542,201, See 37 CFR 1.78(a)(5). The English translation and a statement that the translation is accurate required by 37 CFR 1.78(a)(5) is missing. Accordingly, applicant must supply 1) the missing English translation and a statement that the translation is accurate in provisional application No. 60/542,201 and 2) in the present application, a confirmation that the translation and statement were filed in the provisional application. If 1) and 2) are not filed (or the benefit claim withdrawn by the filing of an amendment or Supplemental Application Data Sheet) prior to the expiration of the time period set in this Office action, the present application will be abandoned. See 37 CFR 1.78(a)(5)(iv).

Information Disclosure Statement

4. Applicant's Information Disclosure Statements filed 4/14/06 and 5/4/06 have been received and entered into the application. The references therein have been considered by the examiner as indicated on the attached form PTO-1449.

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

6. Claims 1-6 and 8-11 are objected to because of the following informalities:

7. In claims 1-4, parts (c), the terminology "is freeze-dried preparation (by freeze drying)" should apparently read --is a freeze-dried preparation prepared by freeze-drying--.

8. In claims 3-4, part (e), "in each the solution" is grammatically correct and unclear. Applicant may intend --in each of the solutions--; however, parts (c) of the claim only refer to "the solution" in the singular. Clarification is needed.

9. In claims 2-4, an article such as --an-- is needed before the word "amount" in parts (d).

10. Similarly, articles are needed before "different kind type of translation template" in parts (e) of claims 3-4. In claim 4 an article is needed before the word "protein" in part (f).

11. In claim 5, the language --The protein chip reagent...of claim 4-- is suggested in place of "The protein chip reagent…according to claim 4" for clarity.

12. Similarly, in claims 6 the language --the protein chip reagent…of claim 1-- is suggested.

13. The word "streptavidin" is apparently misspelled in claim 5.

14. In claims 8-11 the language --the protein chip reagent of claim X-- is suggested.

15. In claims 8-11 the language --A kit for cell-free protein synthesis-- is suggested.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

18. Claims 1-4 recite "low-molecular protein synthesis inhibitors". The claim is indefinite because it is unclear what is meant by "low-molecular". Perhaps Applicant intends "low molecular weight"?

In addition, the term "low-molecular" is a relative term that renders the claim indefinite. The term "low-molecular" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. If "low-molecular" is indeed referring to protein synthesis inhibitors of low molecular weight, the scope of the claim is nonetheless unclear because it is not apparent what molecular weights or ranges of molecular weights would be considered "low" in this context.

For all of these reasons, the metes and bounds of the claim are unclear.

19. Claims 1-4 recite "the substances necessary for protein synthesis" in parts (b). There is insufficient antecedent basis for this limitation in the claims.

20. Claims 1-4 recite "the well mentioned in "a";" in parts (b). There is insufficient antecedent basis for this limitation in the claims because parts (b) of the claims refer to "each different well", which implies that there are multiple wells. Therefore, there is ambiguity as to which of the multiple wells is intended by the reference to "the well".

21. Parts (a) and (b) of claims 1-4 render the claims indefinite because they apparently invoke *process* steps ("…is added to each different well.." in part (a); "…are added to the well…" in part (b)) in the context of *product* claims. Clarification is needed.

22. Claims 2-4 recite the limitation "the protein" in parts (d). There is insufficient antecedent basis for this limitation in the claims.

23. Claims 1-2 recite the limitation "the solution in the well mentioned in "b"…" in parts (c). There is insufficient antecedent basis for this limitation in the claim because part (b) does not refer to a solution. Similarly, claims 3-4 recite "the solution in the well mentioned in "b"…" in parts (c) and (e), for which there is insufficient antecedent basis.

24. Claims 2-4 recite in part (d) that the amount of deliquescent substance is "0.01 part by weight or less to 1 part by weight of the protein". This renders the claims indefinite because the scope of the claims is not clearly set forth. In particular, the reference to "0.01 part by weight or less" would appear to invoke the range of 0-0.01 part by weight. However, the claims then continue "to 1 part by weight", implying an upper limit of 1 rather than 0.01. Furthermore, the reference to "the protein" is unclear. As discussed above, there is insufficient antecedent basis for this limitation as there is no prior mention that the reagent contains a protein. Does Applicant intend to define the amount of deliquescent substance in relation to the amount of protein? Or in relation to the total weight of the reagent? For all of these reasons, is unclear what amounts of deliquescent substance would fall within the scope of the claims.

25. Claims 3-4 refer to "different kind type of translation template" in parts (e). This terminology is vague and indefinite because the specification and claims do not indicate what would be considered a "different" template, i.e. different as compared to what? Perhaps

Applicant intends a plurality of different translation templates? If so, does Applicant intend that different templates are capable of being added to different wells (i.e., one template per well) or alternatively that multiple, different templates are capable of being added to each well? In addition, the recitation of "different kind type" is confusing since the use of the words "kind" and "type" appears to be redundant.

26. Claim 4 recites the limitation "said modification for fixation" in part (f). There is insufficient antecedent basis for this limitation because although the claim refers to the protein being "modified for fixation", there is no recitation of a modification *per se.*

27. Claims 4-5 are indefinite because claim 4 recites that the protein is "modified for fixation" and is also "coated" with a substance that has affinity a substance added by the modification. This language is vague and indefinite and it is unclear what is meant. What is meant by a protein "coated" with a substance? Perhaps Applicant intends that the protein is attached to a substance?

Furthermore, it would seem that the species recited in claim 5 might be considered modifications for the immobilization or fixation of a protein to a surface. Perhaps Applicant intends that the protein is modified by attachment to a substance, so that the protein would be capable of being immobilized? Or is the "modification for fixation" separate and distinct from the "coating" of the protein?

28. Claim 5 specifies the modification is "selected from making into" avidin, biotin, streptoavidin, and his tag. It is unclear what is meant by this terminology. In particular, it is unclear whether the protein is modified by attachment to avidin, biotin, etc., or alternatively whether the protein is being modified by attachment having affinity to one of these species.

Claim Rejections - 35 USC § 102

29. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

30. Claims 1-2, 6, and 8 are rejected under 35 U.S.C. 102(a), in the alternative under 35 U.S.C. 102(e), as being anticipated by Kuroita et al. (US 2003/0199076 A1).

Kuroita et al. teach a reagent composition for cell-free protein synthesis that is provided in a freeze-dried state for stability (the abstract, [0001], [0004], [0006], [0102]). The reagent composition contains (a) a cell extract, which may be from wheat embryo without endosperm and almost free of protein synthesis inhibitors such as ribosome specific glycosidase [0003], [0035], [0055], [0111]. The composition preferably contains (b) a bioactive protein for cell-free protein biosynthesis, an energy source, template mRNA, substrate amino acids, etc., (i.e., substances necessary for protein synthesis) which may be provided in kit form. See [0002], [0027], [0062], [0064], [0089]-[0098].

Regarding the recitation that the reagent components are "added" to wells of a partitioned container, such statements are interpreted as being directed to the intended use of the claimed reagent. The Examiner notes that no structural difference is apparent as a result of this statement of the intended use of the claimed reagent. Therefore, since the components of the freeze-dried

reagent of Kuroita et al. would also be capable of being added to wells of a partitioned container, it meets the claim.

With respect to claim 2, Kuroita et al. further teach that the reagent composition includes an amount of a deliquescent material that is no more than 0.01 part by weight per part of protein [0011], [0024], [0034], [0102]. As discussed above, the reagent composition would be capable of performing the intended use of being added to wells and therefore reads on the claim.

With respect to claims 6 and 8, Kuroita et al. teach kits comprising the reagent composition [0089]-[0091].

31. Claims 3-5 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuroita et al. in view of He et al. (WO 02/14860) and Zuk et al. (4,208,479).

Kuroita et al. is as discussed above, which teaches a template for protein synthesis [0062] but fail to specifically teach that "different kind type of translation template is contained in each the solution mentioned in "b" ". As best understood (see 112, 2nd paragraph issues above), the subject matter claimed relates to the use of multiple, different templates so that the protein chip reagent can be used to synthesize multiple, different proteins. Regarding claims 4-5, Kuroita et al. also fail to specifically teach that the protein synthesized is "modified for fixation" and also "coated with a substance having affinity for a substance added by the said modification". As best understood (see 112, 2nd paragraph issues above), the subject matter claimed relates to attachment substances such as avidin, biotin, etc. to the nascent proteins for the intended purpose of fixation or immobilization on a solid phase.

He et al. teach cell-free protein synthesis systems that employ an array format, allowing the advantage of handling and investigation of multiple samples (pages 1 and 7-8). This allows for protein arrays to be prepared, so that the functions of thousands of proteins can be examined in parallel (ibid). In one embodiment, the in vitro synthesis reactions can be performed in wells of multiwell plates, using individual nucleic acids such as mRNA as starting material (i.e., templates). See page 7.

Therefore, it would have been obvious to one of ordinary skill in the art to include individual templates for protein synthesis as taught by He et al. in the protein chip reagent of Kuroita et al. so that an array of many different proteins could be synthesized by cell free protein synthesis and then examined in parallel. The advantage of handling and parallel investigation of multiple proteins produced by cell-free protein translation provides motivation to combine the teachings of He et al. with those of Kuroita et al., which also relates to cell-free protein translation.

It is not entirely clear what is meant by the template(s) being contained in the solution mentioned in "b" (see 112, 2nd paragraph issues above). However, as best understood Applicant intends that the template(s) are provided together with other components of the reagent.

In this regard, Zuk et al. teach that in performing assays it is a matter of substantial convenience, as well as providing significant enhancement in accuracy to provide the reagents combined in a kit form and preferably in a single vessel (column 22, lines 21-44). Therefore, when taken together with the teachings of Kuroita et al. and He et al. which establish that both wheat germ extract and a template are required for protein synthesis reactions, it would have

been obvious to one of ordinary skill in the art to combine these two ingredients together for convenience and accuracy.

Regarding claims 4-5, He et al. further teach adapting proteins to be synthesized by in vitro translation for rapid isolation, immobilization or identification by inclusion of modifications for fixation (sequences such as hexahistidine or other peptide tags). See in particular the abstract and pages 7 and 12. This allows for the proteins to be captured onto wells or other surfaces that have immobilizing reagents (i.e., substance having affinity to a substance added by the modification).

Therefore, it would have been further obvious to incorporate hexahistidine or other peptide tags as taught by He et al. in the nascent proteins to be synthesized by the protein chip reagent of Kuroita et al. so that the translated proteins could be rapidly isolated, immobilized and/or identified via such modifications.

Put another way, given that He et al. taught that such modifications can be included in proteins being translated in cell-free protein synthesis systems for the purpose of rapidly isolating, immobilizing and identifying the synthesized proteins, it would have been obvious to apply this known technique in order to improve the cell-free protein synthesis system of Kuroita et al. in the same way and achieve the expected results.

Regarding claims 9-11, Kuroita et al. teach kits comprising the protein chip reagent [0089]-[0091] as discussed above. Zuk et al. also teach the advantages of providing reagents together in kit form. Therefore, it would have been further obvious to include the protein chip reagent of Kuroita et al., He et al., and Zuk et al. as part of a kit for the art-recognized benefits of convenience and commercial sale.

Conclusion

32. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

33. Endo et al. (WO 02/24939 and English language counterpart US 6,869,774) teach cell-free protein synthesis in multi-well microtiter plates (see, e.g., column 4, lines 29-30), which is relevant to the intended use of the claimed reagent in being added to microtiter plate wells.

Rothschild et al. (US 6,303,337 B1) is also cited for its relevance to claims 4-5 for its teaching that affinity markers such as avidin or a His tag can be incorporated into nascent proteins during cell-free protein translation for subsequent isolation and detection. See the abstract; column 8, lines 3-21 and column 30.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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